THE ORIGIN AND DEVELOPMENT OF NERVOUS DISTURBANCES EXPERIMENTALLY PRODUCED [1]

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History

The first experimental neurosis [2] produced in animals dates back a quarter of a century to the classical experiments of Pavlov made on the basis of his newly discovered method —that of the conditioned reflex. Like the discovery of the malarial treatment in dementia paralytica by two Russians in 1888—forty years before its general use—and the early reports of the use of sulphanilamid, these experiments of Pavlov attracted no attention until recently when they have been used by a good many workers in this country on various animals—from the rat to the primates. Pavlov showed that the disturbances in animals were manifested by an imbalance in the conditioned reflexes as well as by certain motor phenomena, and the workers in this country have been able to see in a variety of animals disturbances of behavior parallel to what Pavlov saw in dogs, *e.g.*, Liddell in sheep, pigs and goats; Maier in rats; Masserman and Dworkin in cats, etc.

Present Work

In addition to the production of the so-called experimental neurosis, the credit for which should go to Pavlov, I have extended this study along three main lines:

I. The production of a chronic anxiety-like neurosis, more properly a state of imbalance situationally determined, produced in 1933, which has lasted now for eight years in one dog.

II. The early detection of the breakdown by measurements of autonomic functions (secretory, cardiac, respiratory, sexual) with the animal under artificial strain. Such measures may reveal a disturbance long before there is a demonstrable change in overt behavior.

III. A study of such a state of imbalance not only upon the CRs but the extension of this imbalance to involve many and various physiological systems—digestive, respiratory, circulatory, urinary, sexual, muscular activity as well as social relationships.

Method

The classical Pavlovian method was exposure of the animal to a difficult problem based upon a strong excitation. Practically this is carried out as follows: a strong food excitation is set up in a hungry animal; the giving of food is preceded by a signal over any receptor system so that the signal later acquires the function of producing the food excitation without the food—the conditioned food reflex. Next an inhibitory process is formed on the basis of the food excitation by some such method as the giving of a signal similar to the first one but always failing to reenforce it with food, until the animal reacts positively to the signal accompanied by food and negatively to the similar signal unaccompanied by food.

Conflict

The next step in the production of the nervous state is the conflict between the signal for the positive activity (excitation) and the negative (inhibition). This may be carried on to the point where the dog is unable to react correctly, to make a differentiation. For example we may use two tones so close together in pitch that the nervous system is physically incapable of discriminating—say 1000 as signal for food and 1012 as signal not accompanied by food. I shall omit discussion of the theoretical considerations—

[1] Read at the ninety-seventh annual meeting of The American Psychiatric Association, Richmond, Va., May 5-9, 1941.

[2] By the term neurosis no attempt is made to identify the state with what is clinically known by the same term. As experimental neurosis is the term introduced by Pavlov it is retained here.

whether the correct explanation is a physical one of overlapping of cortical processes of excitation and inhibition, or whether the conflict is based on a more highly organized psychobiological level, such as is indicated by "frustration." The essential element seems to be a difficult situation based upon a strong excitation.

Many other methods may be used, involving in general either a natural emotional shock (intense fear, fights, etc.), a difficult change in routine, or conflicting stimuli leading to opposite reactions.

Acute Conflict

The behavior of any dog can be upset temporarily by such a conflict as described above. This is expressed in his general behavior (restlessness, etc.), by a loss of equilibrium between all the CRs (changing the relative intensities, *e.g.*, over-reacting to some, under-reacting to others), and finally, as we have been able to show recently by records of the heart rate and respiration, in emotional changes.

Acute Breakdown

An incipient nervous imbalance may be detected by measuring the departure from normal in certain autonomic responses—in the secretion, the cardiac frequency, the character and rate of respiration, the sexual reflexes under constant stimulation. In order to detect an abnormality one must first establish the normal laws governing each one of these functions. This I have done for the secretion and the heart rate. Regarding the salivary secretion I have determined that the relation of the conditioned salivary secretion to the strength of unconditioned stimulus (amount of food) is an exponential function; the conditioned reflex can now be expressed by a formula, viz.,

$$CR = a + b\,(1 - e^{-cQ}),$$[3]

where a, b, c are constants for a given dog, e the base of natural logarithms, and Q the quantity of food (Chart I). If there is a departure from this formula in the salivary secretion, we have an indication of a nervous disturbance. In the following dog (Kompa) the effect of introducing a new and undifferentiated stimulus is seen on the other conditioned reflexes. They fall to zero soon after the new (confusing) stimulus (M_{144}) is given; they gradually return to normal size during a period of 10 minutes or more (see Chart II).

The heart rate, as has been shown in my

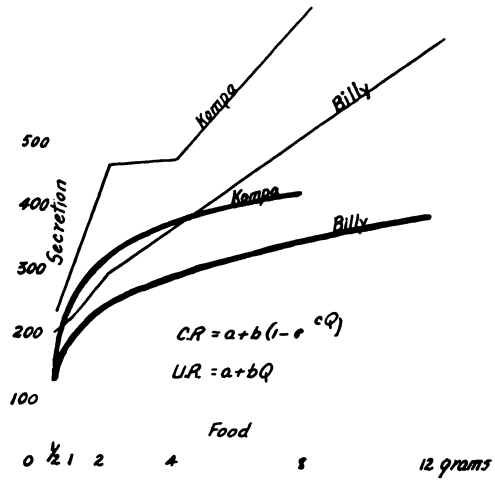


Chart I.

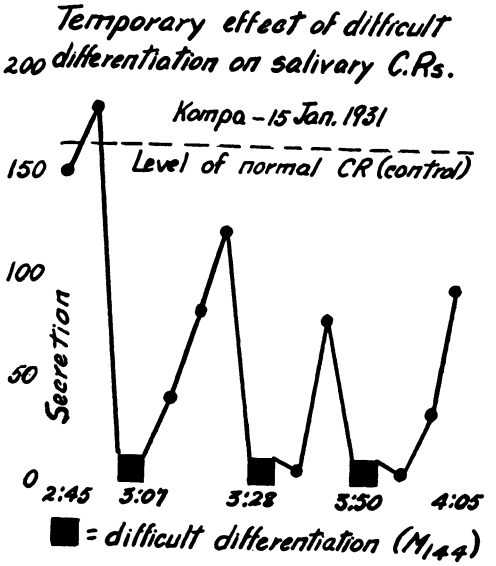


Chart II.

[3] Gantt, W. Horsley: The nervous secretion of saliva: the relation of the conditioned reflex to the intensity of the unconditioned stimulus. Am. J. Physiol., vol. 123, no. 1, p. 74, July, 1938.

laboratory,[4] bears a quantitative relationship to the intensity of the conditioned stimulus and to inhibition: it is larger for a signal denoting a large amount of food than it is for a signal which has habitually accompanied a small amount of food, and there is still another rate for an inhibitory stimulus. This has been established for both painful and food stimuli (Chart III). With a difficult differentiation, a situation which the animal cannot solve nor escape from, these normal relations of the cardiac reflexes become exaggerated or chaotic as can be seen in the following dog. A comparison of the heart rates in this dog in December when he was able to differentiate and in January when a new stimulus was introduced which he could

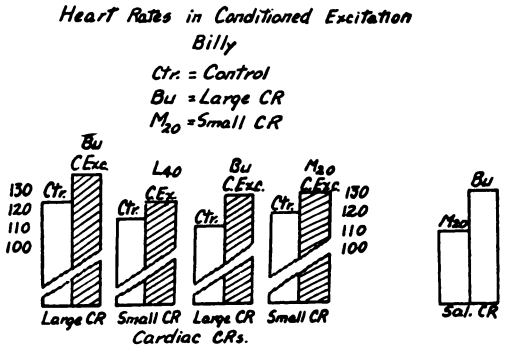


CHART III.

not differentiate shows the accompanying change in the heart rates.

The next charts illustrate the respiratory changes accompanying good differentiation, as compared with the irregularity and upheaval in the respiration in the same dog before differentiation is accomplished (Charts IV and V).

Similarly a single introduction of a new stimulus, *e.g.*, a flashing light for 10 seconds, may cause in susceptible dogs a profound effect on the sexual reflexes measured soon after the use of this disturbing light. The following chart shows how the sexual reflexes have been reduced to zero by such a stimulus (see Chart VI).

In certain animals such a temporary imbalance may become chronic. The two chief factors seem to be (1) the constitution of the individual, and (2) the severity of the conflict.

CONSTITUTION

Whether an animal will show a permanent disturbance under strain, as well as the extent of the disturbance in behavior and in the

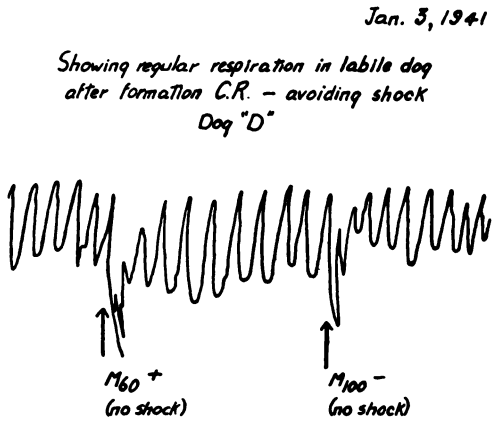


CHART IV.

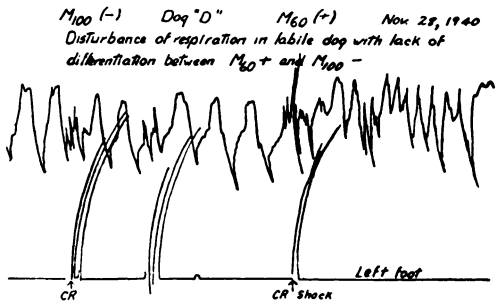


CHART V.

autonomic system depends upon the stability of the animal. Three animals were subjected to identical situations of conflict—the differentiation of two tones of 1012 and 1024. All three showed temporary disturbances. One of these developed a chronic and apparently incurable neurosis, while the other two could be promptly cured by appropriate means.

DEVELOPMENT

The pathological animal showed not only an acute disturbance, but a series of developments which have continued for a period of

[4] Gantt and Hoffman: Conditioned cardio-respiratory changes accompanying conditioned food reflexes. Am. J. Physiol., vol. 129, no. 2, pp. 360-61, May, 1940.

nine years since the original conflict. The animal was subjected to the difficult differentiation for several months in 1932; bring ing him into the experimental environment since then has apparently been sufficient to induce the spread of the neurosis to new physiological systems ("Nick").

General Behavior

The food excitation passed over into one of defense, characterized by resistance to

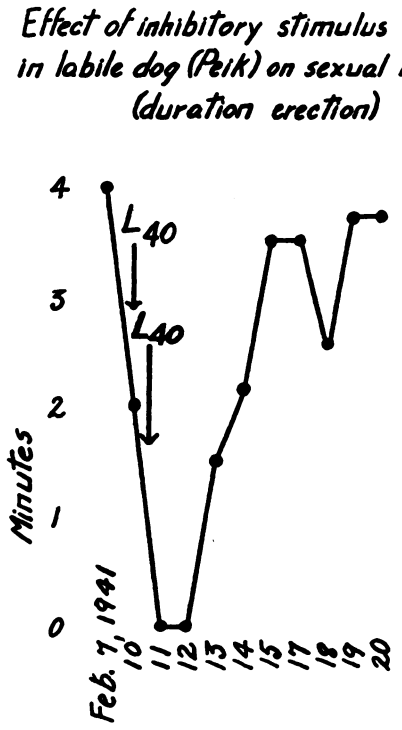


Chart VI.

being brought into the environment and panicky fear reactions of a severe degree.

The animal exhibits all the symptoms to a former signal for food that an ordinary dog does for actual pain, viz., whimpering, howling, retreating, rapid panting, tachycardia.

Any new element brought into the old environment and closely associated with it acquires the function of producing the nervous state. Thus not only the conditioned signals originally used in the environment, but any new one introduced even after several years during which there has been no actual conflict, may acquire the property of bringing on all the symptoms. For example, a flashing light, which had never been used before and which was without effect the first time employed, after 8-10 combinations of light with tone, evoked almost the identical responses as the tone itself (Chart VII).

Gastrointestinal System

The environment and particularly the specific stimuli used exert an inhibitory influence on all the conditioned food reflexes. The secretion of saliva to food is inhibited. It is safe to assume that also the gastric secretion and the pancreatic, which is initiated by the gastric secretion, as well as the concomitant expulsion of bile, suffer in the same

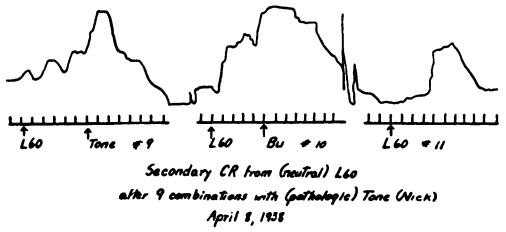


Chart VII.

way. It is important to note, however, that the secretions which are not dependent upon the cerebral cortex are not inhibited, such as the unconditioned reflex and chemical secretions.

Respiration

Two years after the original conflict the animal began to show (1) a respiratory tic when he was brought into the environment or even approached it (this consisted in loud, raucous, and prolonged expirations and inspirations); (2) marked changes in respiration followed any of the signals used in the original environment, or (3) even those which were later associated with it, as shown in Chart VII.

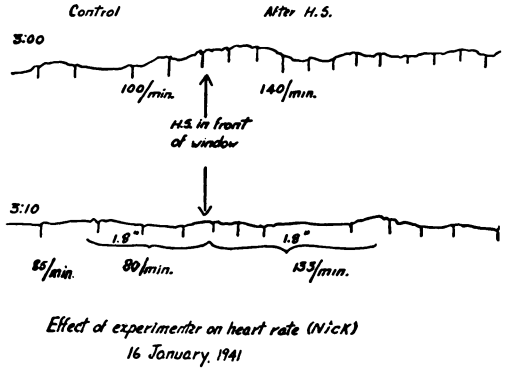
Heart Rates

In the experimental environment the heart rate is constantly elevated, ranging between 130 to 205, with exacerbations when any of the original signals are used (Chart VIII). When this dog was removed from the ex-

perimental laboratory to a farm life his heart rate dropped about 50 per cent (95 to 130). A normal dog shows a slightly increased heart rate during the CR for food—from about 110 to 125.

Micturition

Intractable pollakiuria is present in the experimental environment, beginning about two years after the conflict, sometimes as much as thirty times in an hour. It is extremely rare that a normal dog urinates in the experimental room or on the stand, even though he may be kept there for 7 hours or more. However, one of the most neurotic of our dogs begins urinating frequently anywhere and everywhere in the environment of



Effect of experimenter on heart rate (Nick) 16 January, 1941

Chart VIII.

conflict, and even aggressively, on the same type of food which was used 5 years previously to produce the conflict. One might easily draw a parallel here to the enuresis of nervous children.

Sexual Reflexes

Reciprocal relations have been noted in several neurotic dogs between the sexual excitation and the anxiety state described above. Normal sexual relations had a temporary dissipating effect upon the neurosis. Secondly in the experimental environment neurotic dogs show, on the one hand, frequent and almost constant erections reactive to the environment and particularly the specific signals formerly connected with food and the difficult problem, sexual erections appearing within a few seconds after a conditioned signal. On the other hand, a condition of ejaculatio præcox is seen in the environment of conflict during adequate sexual stimulation. In normal dogs the working environment has no effect upon the onset and duration of erection to normal stimuli, while in this animal the onset and duration were decreased by the environment to about one-third of what they were outside the environment.

Social Relationships

The presence of the observer also has a temporary dissipating effect upon the anxiety-like state. The dyspnea disappears, the animal is quiet, and the fear reaction may be completely abated, or delayed until the human companion leaves the room. The close proximity and especially petting by almost

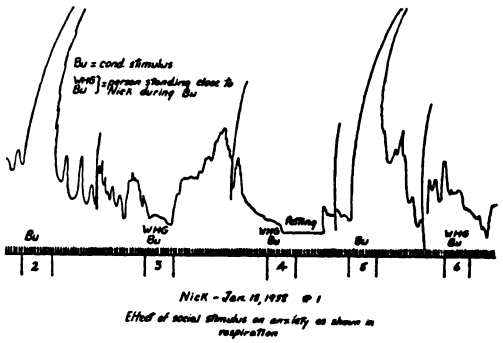


Chart IX.

any human subject has this beneficial effect whereas the presence of another dog, except for special "friends," does not have this specific effect (Chart IX).

Activity

The 24-hour activity of the animals which have become neurotic does not differ in amount from the normal—it may be either exaggerated or diminished, depending upon the type of dog. However we have shown that an interesting correlation in activity exists between normal dogs that is not present between the neurotic and the normal dogs.[5] Thus the normal dogs show parallel

[5] Gantt and Muncie: Rhythmic variations of gross muscular activity in dogs correlated with secretion and with conditioned reflexes. Proc. Am. Physiol. Soc., Apr., 1941, p. 99.

fluctuations in their activity when placed in adjacent cages, but the activity of the neurotic dog is independent of those surrounding him, to the extent that there is no positive correlation.

mental room in that period. After two months in the country in 1937 the dog showed a marked improvement—diminished heart rate, quieter respiration, less whining and defense reactions, less pollakiuria. This

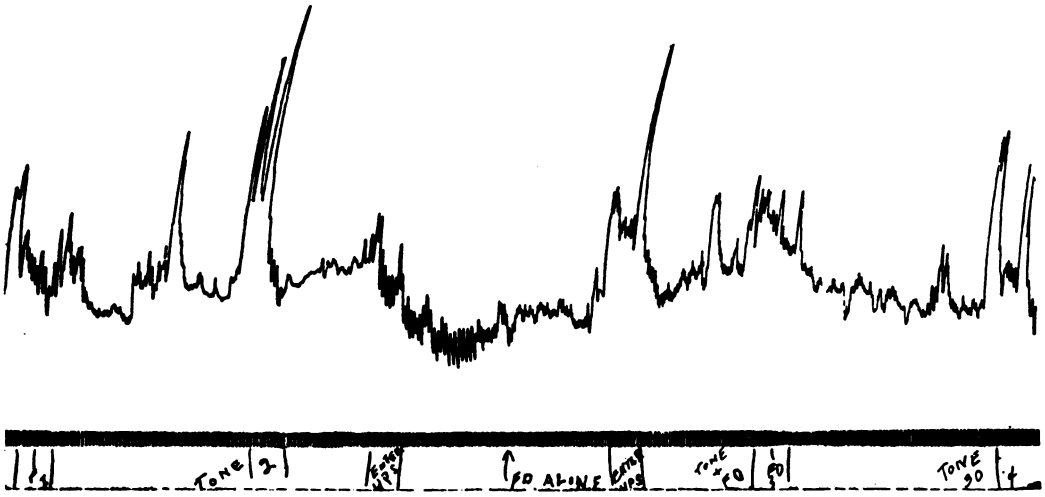


CHART X.—Changes in respiration on May 25, 1937 to pathological stimulus, tone. (Dog Nick.)

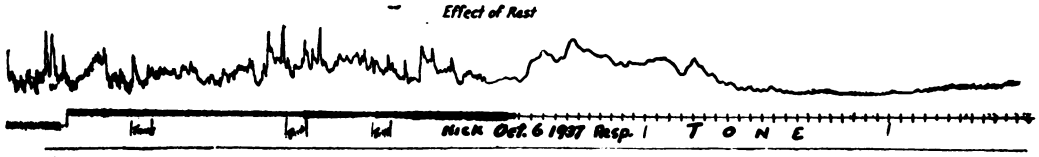


CHART XI.—Showing effect of rest in country on respiratory reaction to pathological tone one day after return of Nick to laboratory.

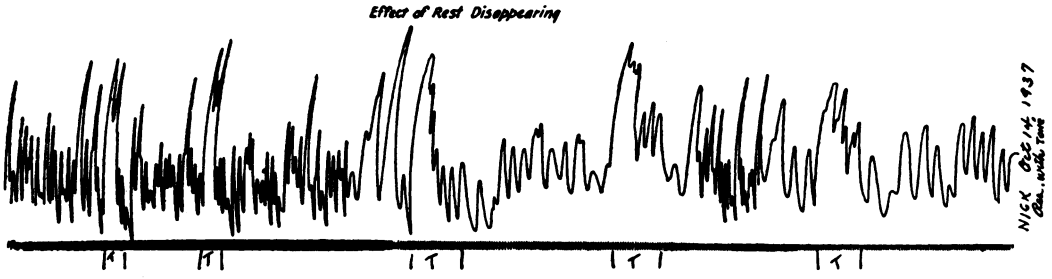


CHART XII.—Showing reappearance of pathological respiratory reaction to tone on Oct. 14, 1937, two weeks after return of Nick to laboratory.

THERAPY

A pronounced improvement was obtained by removal of the dog to an entirely new environment—to a farm. The improvement could not be obtained by 18 months' rest in the laboratory environment, even though the dog was not brought down into the experi-

condition lasted for several weeks after the dog was returned to the laboratory environment, but in that environment the symptoms gradually reappeared. The following 3 charts show: the respiration before rest in the country (Chart X), one day after his return to the laboratory (Chart XI) and two

weeks and six months later (Charts XII, VII).

A longer rest in the country, 18 months (1939-40) had a greater effect in reducing the abnormal symptoms. While on the farm he gradually became almost normal except for a few relapses. After returning to the laboratory in January 1941 this neurotic dog (Nick) has shown a great improvement,

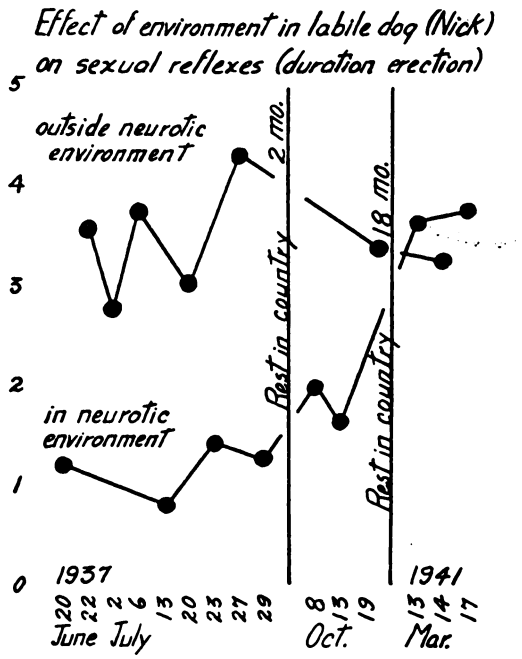


CHART XIII.

though almost all of his old symptoms reappeared in the experimental room, but in a lesser degree. Chart XIII illustrates the effect of rest on the sexual reflexes.

Other attempts to modify the environment had only a temporary effect. One of the measures used was transformation of the environment from unpleasant to pleasant by giving him all of his daily rations for several months in the experimental environment and none outside; this had an ameliorating result only during the period that the dog was being fed there.

CONCLUSION

The most striking features in this study have been the importance of the individual and the extension of the effects of the conflict for years after its original use as well as the extension to new systems later during the life of the dog.

The most important therapeutic indication is the detection of susceptible animals by measuring the reactions under strain, and preventing the progress of the strain to that point at which a permanent breakdown occurs. Once the disturbance is thoroughly established, therapy is difficult. Improvement has been seen with a complete change of environment—removal to farm life for 18 months. Rest in the environment of conflict was unavailing.

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